

Fig. 1

1 CAGCTCTCAT TTCTCCAAA ATGTGTTTGA GCCACTTGGA AATATAGCCT TTAAGCCATT CAAGAACTCA AGGAGCTCAG AGATCATCCT GGAAGCTGTG
 CTCGAGAGTA AAGAGGTTTT TACACAACCT CGGTGAACCT TTATATACGA AATTGCGTAA GTTCTTGAGT TCCTCGAGTC TCTAGTAGGA CCTCGACAC
 1 MetCysLeus erHisLeuGI uAsnMetPro LeuserHis exArgThrGI nGlyAlaGI nArgserSer rPlySLeuTrp

101 GCTCTTTTGC TCAATAGTTA TGTGCTATT TCTTTGCTCC TTCAGTTGGC TAATCTTTAT TTTTCTCCAA TTAGAGACTG CTAAGGAGCC CTGTATGGCT
 CGAGAAAACG AGTTATCAAT ACAACGATTA AGAAACGAGG AAGTCAACCG ATTAGAATA AAAAGAGGT AATCTCTGAC GATTCTCGG GACATACGA
 28 LeupheCys SerileValm etLeuLeuph eleuCysser PheserTrpL euilePheIl ePheleuGI nLeudluThra lalySgluPr ocysMetaIa

201 AAGTTTGAC CATTACCCTC AAAATGGCAA ATGGCATCTT CTGAACCTCC TTGGGTGAAT AAGGTGCTG ACTGGAAGCT GGAGATACTT CAGAATGGCT
 TTCACAACCTG GTAATGGAG TTTTACCCTT TACCCTAGAA GACTTGGAGG AACGCACTTA TTCCACAGAC TGACCTTCGA CCTCTATGAA GTCTTACCGA
 LyspheGlyP roleuProse rlyStrpGI nMetaIasers ergluProPr ocysValasn LysValsera sPTripLysle uGIuleleu GIasnGlyLeu

301 TATATTTTAT TTATGGCCAA GTGGCTCCCA ATGCAAACTA CAATGATGTA GCTCCTTTTG AGTGCGGCT GTATAAAAAC AAAGACATGA TACAACCTCT
 ATATAAATTA AATACCGGT CACCGAGGT TACGTTTGA TTTACTACAT CGAGGAAAAC TCCACGCCGA CATATTTTGG TTCTGTACT ATGTTTGA
 95 TyrLeuIl etYrglyGI nValAlaProa snAlaAsnTy rAsnAspVal AlaProPheG luValArgle uTyrLysAsn LysAspMetI leGI nThrLeu

401 AACAAACAAA TCTAAATCC AAAATGTAGG AGGACTTAT CAATTGCATG TTGGGGACAC CATAGACTTG ATATTTCACT CTGAGCATGA GCTTCTAAA
 TTGTTTGTGT AGATTTTACG TTTTACATCC TCCCTGAATA CTTAACGTAC AACCCCTGTG GTATCTGAAC TATAAGTTGA GACTCGTAGT CCAAGATTTT
 128 ThrAsnLys SerLysileG lAsnValGI yGlyThrTyI GlueuHisv alGIyAspTh rIleAspleu IlePheAsns ergluHisGI nValLeuLys

501 AAATTAATCAI ACTGGGGTAT CATTTTACTA GCAATCCCT AATTCACTTC CTAGAGACTT GATTGTGATCT CCTCAATCCC TTCAGACAT GTAGAGGTGC
 TTATTTATGA TGACCCCATTA GTAATATGAT CGTTTAGGGG TTAAGTAGAG GATCTCTGAA CTAAACTTGA GGAGTAAGGG AAGTGTGTA CATCTCCACG
 161 AsnAsnThrT yTrpGlyI l eileLeuAlaAsnProG l nPheIlese rAM*

601 CAGTGGGTG ATTGAGGGA GAAGATATTC AATTCTTCTA GTTTGTCTGT CTACAAAAT CAACACAAC AGAACTCCTC TGCAAGTGAA TTTTCATCTA
 GTCAACCCACC TAACCTCCCT CTCTATAAG TTAAGATCT CAACAGACA GATGTTTTTA GTTGCTTTG TCTTGAGGAG ACGTGCACTT AAAAGTAGAT

701 TCATGCCCTAT CTGAAGAAGA CTCAGGGGAA GAGCCAAAAGA CTTTGTGTG GATCTGCAGA AATACTTCAT TAATCCATGA TAAACCAAT ATGATGACA
 GTACGGATA GACTTTCTCT GAGTCCCTCT CTGGTTTCT GA AAAACCAAC CTAGACGTCT TTATGAAGTA ATTAGGTACT ATTTGTTTA TACCTACTGT

801 GAGGACATGT GCTTTTCAA GAATCTTTAT CTAATCTCTG AATTCATGAG TGA AAAAATG GAGTTCTATT CCCATGGAAG AATTACCTGG TATGCAAAAA
 CTCCTGTACA CGAAAAGTTT CTTAGAATA GATTAAGAAC TTAAGTACTC ACCTTTTTAC CTCAAGATTA GGGTACCTTC TAAATGAGCC ATACGTTTTT

901 GCACTGGGG CAGTAGCCTG GCTTTGTCTCT CATATCTCTG GCCTGCTGTA ATTCACTCTT CTCATCTCC CATCTTCTGA GACCCCTCCA ATAAAAAGTA
 CCTAGACCCC GTCATCGGAC CGAAAACAAGA GTATTAAGAAC CCGACGACAT TAAGTAAGAA GAGTATGAGG CTAGAAGACT CTGGGAGGGT TATTTTTCAT

1001 GACTGATAGG ATGGCCACAG ATATGCCCTAC CATACCCTAC TTTAGATATG GTGGGTGTAG AAGATAAAGA ACAATCTGAG AACTATTGGA ATAGAGGTAC
 CTGACATPCC TACCGGTCTC TATACGATG GTATGGGATG AATCTATAC CACCACAATC TTCTATTTCT TGTATGACTC TTGATTAACCT TATCTCCATG

1101 AAGTGGCATA AAATGGAATG TACGCTATCT GCAATTTCT CTGGTTTTTA TCTTCTCAG GATGACAGGT GCTTTAAAAA GCCTTATCAA AGGAGTCATT
 TTACACCTAT TTACCTTAC ATGCAATPAG CCTTTAAGA GAACCAAAAT AGAAGAGTCC CTACGTTCCA CGAAATTTTT CGGAATAGTT TCCCTCAGTAA

1201 CGGAACCCCTC ACGTAGACTT TTGTCAGACC TTACTGTTCG TGTGTCGTC TAAACATTCG TAATTTGTA GAAGAGTAA CCATTAGTAA TCATTAGGTT
 GGCTTGGGAG TGCATCTCGA AACACTCTGG AATGACAAC TATATGTAAG TATTTGTAAG TATTTGTAAG TATTTGTAAG TATTTGTAAG TATTTGTAAG

1301 TAACCCAGCA ATGTAATTAT CATTACTGCA TTAATGCAAT TAATGATTTA GAAATTTTAC CTAGCTTCC ACAGTTTGA AAGTGCCTTC GTAACACGT
ATTGGGCTCT TACCAATAATA GTAATGACCT AATACAGTAC ATTACTAAT CATTAATAATC GATCGAAGG TGTCAAAAGT TTCAAGAAAG CATTTTGTCA
1401 TAGCAATTCCT ATGAAGTTAA TTGGGCAGGC AATTGGGGGA AAATTTTACT GATGAGATG TGAATAGCATA GCATAGCCAA CTTTCCCTCA CTCATAGGAC
ATCGTTAAGA TACTTCAATT AACCCGTCCG TAAACCCCTT TTTAATAATCA CTACTCTTAC ACTATCGTAT CGTATCGGTT GAAAGGAGTT GAGTATCCTG
1501 AAGTGACTAC AAGAGCAAT GGTAGTCCC CTGCATGCA CTGTCTCAGC TTTAGAATTG TTAATTTCTGC TATCGTGTTA TAAGACTCTA AAACCTTAGC
TTCACGTGATG TTCTCCGTTA CCCATCAGGG GACGTAACTT GACAGAGTCC AAATCTTAAC AATAAGACG ATAGCACAAT ATTCTGAGAT TTGGAATCCG
1601 AATTCACTTT TCAGGAAGCA TATTCCTCTT TAGCCCAAGG TGAGCAGAGT GAAGCTTTC CTATACAGC ACACCTTTT TTTTCTTCC
TTAAGTGAAA AGTCCCTTCGT ATAAGGGGA ATCGGCTTCC ACTGCTCTCA CTTCGATGTT GTCTAGAAAG GAAATGCTG TGTGAAAAA AAAAAAAGG
1701 TGCCTGAATC AGGAGATCC AGGATGCTGT TCAGGCCCAA TCCCAACCAA ATTCCCTTT TCACCTTGA GGGCCCATCT TAGTCAATG TGCTACTTC
ACGACTTAG TCCCTCTAGG TCCCTACGACA AGTCCGCTTT AGGCTTGCTT TAAAGGGAAG AGTGAACGT CCGGGGTAGA ATCAGTTTAC ACGATTGAAG
1801 TAAATATAATA AATAGCACA ATTCAAAATT TTTGGAATCT TAAATTAGCT ACTTGCTGCTG AAGGNATATA ATGATTACAT TGTAAACAAA
ATTTTATTTAT TTATCGTGAT TAAATTTTAA AAACCTTAGA ATTTAATCGA TGAACGNCCA ACGAACAACT TTCCNTATAT TACTAATGTA ACATTTGTTT
1901 TTTTAAATAT TTATGATAT TTGTGAAGG CTGCATTAAT TTAATAATA TTAACATGTA AGCT
AAATTTTATA AATACCTATA AACACTTTTC GACGTAATAC AATTATTTAT AATGTACATT TCGA

Fig. 1 (cont.)

		<u>A</u>		<u>A'</u>	<u>B'</u>
DNA 19355	52	ETAKEPCMAKFG-----	PLPSK---	WQMASSE	PCVNKVSDWK--
TNF- α	84	PSDK-PVAHVVA-----	NPQAE	QLQ----	WLNRR-ANALLANGVELRDNQ
Apo2L	119	GPQR-VAAHITGTRGRSNTLSSPNSKNEKALGRKINSWESSRSGHSFSLSNLH-LRNGE			
CD95L	142	E-LR-KVAHLTG-----	KSNSRSM-PL	-----	WEDTY-GIVLLS-GVKYKKGG
LT α	59	STLK-PAAHLIG-----	DPSKQN-SLL-----	WRANT-DRAFLQDGFSLSNNS	

		<u>B</u>	<u>C</u>	<u>D</u>	<u>E</u>
DNA 19355	86	LEILQNGLYLIYGQVAPNAN-----	YNDVAPFEVR	LYKNK-DMIQTLTNK-SKIQN	
TNF- α	124	LVVPSEGLYLIYSQVLFKGQGCP----	STHVLLTHTISRI	AVS---YQTKVNLLSAIKS	
Apo2L	175	LVIHEKGFYIYSQTYFRFQEEIKENTKNDKQMVQYIYKYTSYDPPI--LLMKSARNSC			
CD95L	182	LVINETGLYFVYSKVYFRGQSC-----	NNLPLSHKVYMRNSKY--	PQDLVMMEGKMMS	
LT α	99	LLVPTSGIYFVYSQVVFSGKAYSPKATSSPLYLAHEVQLFSSQYPFHVPLL-SSQKMVY			

		<u>F</u>	<u>G</u>	<u>H</u>
DNA 19355	136	-----VGGTYELHVGD	TIDLIFNSEHQVLKNNT-YWGIILLANPQF-IS	
TNF- α	176	PCQRETPEGAEAKPWYEPIYLGGVFQLEKGDRLSAEINRPDYLDFAESGQVYFGIIAL		
Apo2L	232	-----WSKDAEYGLYSIQCGIFELKENDRIFVSVTNEHLIDMDHEA-SFFGAFLVG		
CD95L	233	-----YCTTGQMWARSSYLGA	VFNLTSA	DHLYVNVSELSLVNF-EESQTFFGLYKL
LT α	157	-----PGLQEPWLHSMYHGAAFQ	LTQGDQLSTHTDGIPHLVL-SPSTVFFGAFAL	

Fig. 2

Fetal
Human

Human 1
Adult

Human 2
Adult

Cancer

FB
-9.3
-7.3
-4.4
-2.4
-1.35

Kidney
Liver
Lung
Brain

Pancreas
Kidney
Sk. muscle
Liver
lung
Placenta
Brain
Heart

PBL
COLON
SM. INTEST
OVARY
Testis
prostate
Thymus
Spleen

G-361
A549
SW480
Raji
MOLT-4
K-562
Hela S3
HL-60

09495368 111898

Fig. 3

09496356-11499

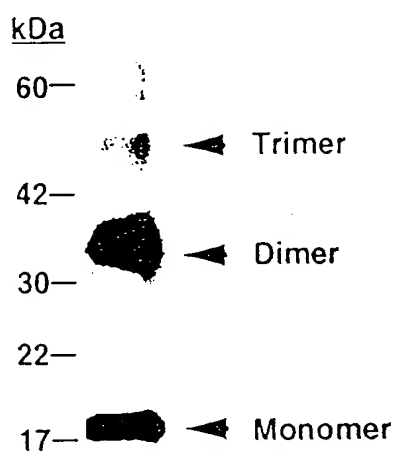


Fig. 4

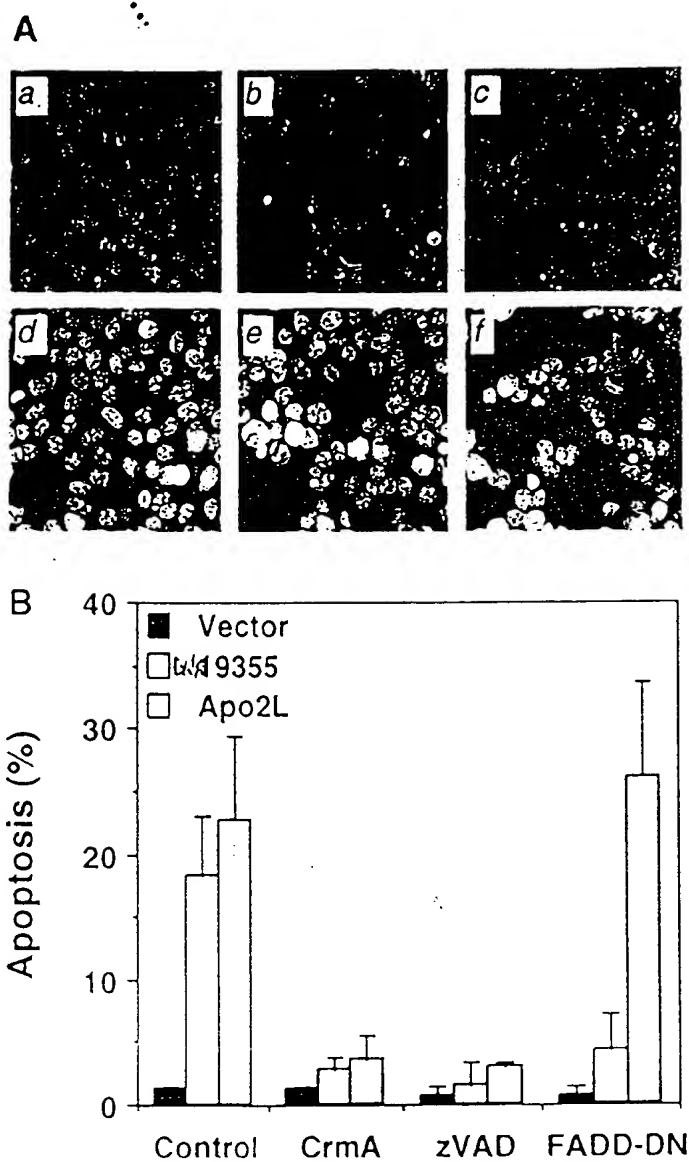


Fig. 5

36347-8936760

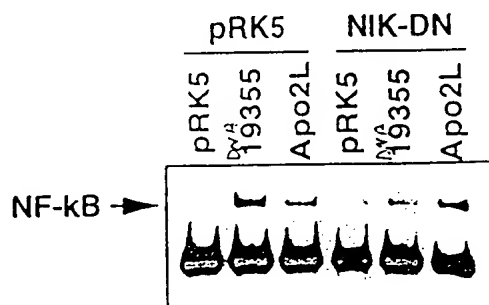


Fig. 6

hG ITR 1 MAQHGA **MGAF**RA**LCGL**AL**LCAL**S**LGOR**P-TGG **PGCGPG**RLL**LG**T**GTDA**RC
 mG ITR 1 - - - - - **MGAW**AM**LYQV**SM**LCV**L**D**L**GQ**PSVVEE **PGCGPG**KVQ**NGSG**NNT**RC**
 hG ITR 50 **CRVHTTRCCRDY****PGEECCSEWD****CMCVQPEFHCGDP****CCTTCRHHPCPPGQG**
 mG ITR 45 **CSLYA**- - - - - **PGKEDCPKERCICVTPEYHCGDP****QCKCKHYPCQPGQR**
 hG ITR 100 **VQSQGKFS****PGFQCIDCASGTFS****GGHEGHCKPWTDC****TQFGFLTVEPGNKTH**
 mG ITR 88 **VESQGDIVFGFR****CVACAMGTFS****AGRDGHCR**L**WTNCS****QFGFLTMEPGNKTH**
 hG ITR 150 **NAVCVPGSP****PAEPLGWLTVVLLA****VAAACVLL**L**TS**A**QLGLHIWQLRSQCMWP**
 mG ITR 138 **NAVCIPEPL****PTQYGH**L**TVIFLV****MAACIFF**L**TTVQLGLHIWQLRRQHMC**P
 hG ITR 200 **RETQLLL****EVPPSTEDARS****COFP****EEERGE**RS**AEEKGR**L**GDLWV**
 mG ITR 188 **RETQPFA****EVQL****SAEDACS****FQFP****EEERGE**Q-T**EEKCH**L**GGRWP**

CRD1
 CRD2
 CRD3
 T M

Fig. 7

09105369-44898

CD95-Ig
DR4-Ig
DR5-Ig
TNFR1-Ig
TNFR2-Ig
Apo3-Ig
h-GITR-Ig
Control

22 Kda
17 Kda

Fig. 8

B

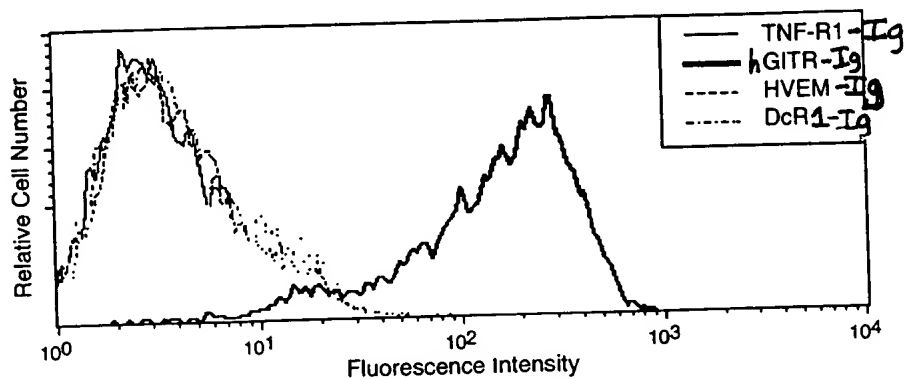


Fig. 9A

C

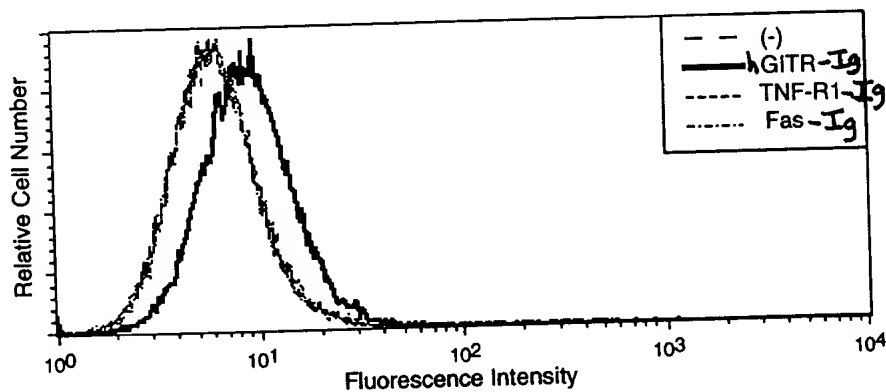


Fig. 9B

35811-39396T60

Transfected	Expression Vector	Relative Luciferase
-	-	~1.0
-	+	~1.0
+	-	~4.8
+	+	~26.0

Fig. 10

36377-89660

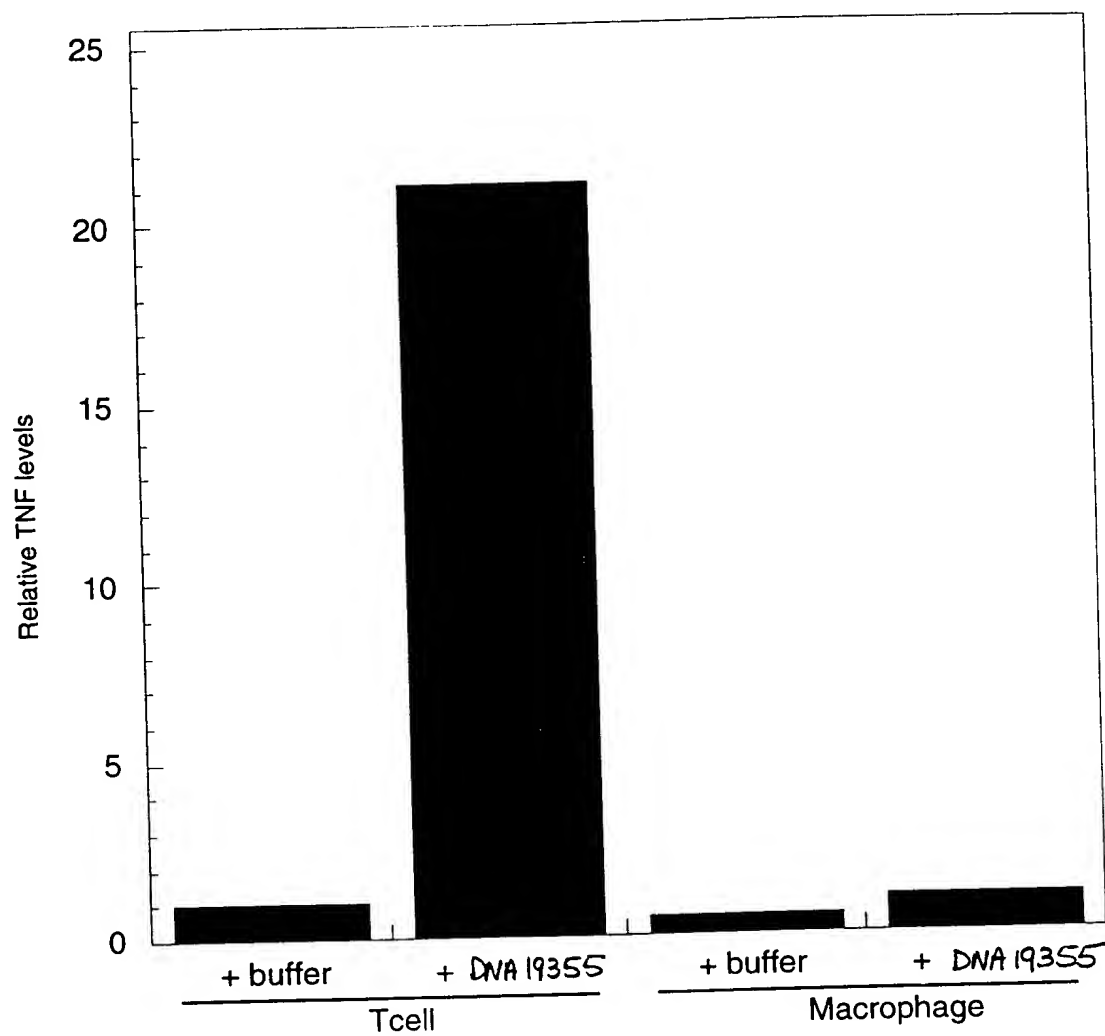


Fig. 11